Summary Report and Presentations

Innovative Diagnostic and Prognostic Tools for the Management and Treatment of Patients with Multiple Myeloma and Myeloma Precursors.

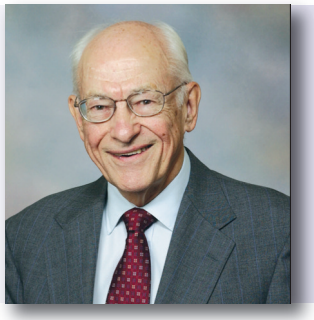
Monitoring Multiple Myeloma in 2012: Implications in Clonal Evolution.

2012 Friday Satellite Symposia (FSS) Preceding the American Society of Hematology (ASH) 54th Annual Meeting

Friday, December 7, 2012
Atlanta, USA

Monitoring Myeloma (M-Proteins) in 2012

Robert Kyle, MD, Mayo Clinic, Rochester, Minnesota, USA



Dr Bob Kyle is a perfect speaker to review the natural history of myeloma, from MGUS (Monoclonal Gammopathy of Undetermined Significance) and Smouldering Multiple Myeloma to Multiple Myeloma. His presentation covers the laboratory methods used for monoclonal proteins and the scientists and physicians who played a major role in their discovery and development.

He includes a historical review, from the first observations of Henry Bence Jones over 150 years ago to the development of serum free light chain assays (**Freelite**®) in 2001. Current laboratory methods for the detection of monoclonal proteins in the serum and urine are considered, with special emphasis on the role of electrophoresis, immunofixation and serum free light chain assays.

Download Monitoring Myeloma (M-Proteins) in 2012
– video and slides

Monitoring, Prognosis and Treatment of Smoldering "Early" Myeloma: New Opportunities

Neha Korde, MD, National Institutes of Health, Bethesda, Maryland, USA

Published data shows that most symptomatic monoclonal gammopathies are preceded by MGUS or Smouldering Multiple Myeloma (SMM). However, the percentage of MGUS and SMM patients progressing to a symptomatic condition each year is relatively low.

To identify which patients are more likely to progress it is important to have accurate risk models. Two have been proposed: Mayo Clinic and Salamanca PETHEMA models. The risk factors differ somewhat in these 2 models and, when applied to a group of SMM patients, there was poor overall agreement in the numbers of patients at low, intermediate or high risk. However in their original studies both models showed around 75% of the SMM patients identified as high risk did progress to a symptomatic monoclonal gammopathy within 5 years (on average in <2 years).

The current standard of care for MGUS and SMM is still observation and careful monitoring only. In 2010, the International Myeloma Working Group recommended that high risk SMM patients should be considered for preventive clinical trials. The IMWG used the 3 risk factor Mayo Clinic model (**Freelite** κ/λ ratio <0.125 or >8, M-protein >30g/L and >10% abnormal plasma cells in the bone marrow).

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Neha Korde, MD, National Institutes of Health, Bethesda, Maryland, USA

One of the reasons for treating patients before progression is to inhibit tumour growth at a time when clonal heterogeneity within the tumour is minimal, thus hopefully reducing the chances of relapse via different clones.

Currently there are several such on-going trials. In one mature trial (Revlimid® & Dexamethasone versus Observation) the patients in the treatment group showed significant benefits for time to progression of disease and overall survival.

Dr Korde concludes that emerging strategies and markers to monitor SMM patients in the future may include:

- Gene expression profiling (Signal Genetics)
- PET/CT scans before and after treatment
- Flow cytometry and PCR to determine minimal residual disease
- Circulating proteasomes.

For confidentiality reasons, video footage and slide presentations are not available for this talk.

The Sub-clonal Nature of Multiple Myeloma: New revelations to Genetic Studies and Biomarker Research

Dr Rafael Fonseca, MD, Mayo Clinic, Scottsdale, Arizona, USA

Our understanding of the sub-clonal nature, or the clonal heterogeneity, of multiple myeloma has grown with the availability of gene expression profiling (GEP) and improved biomarker assays. The clinical implications of tumour heterogeneity mean:

- Changing responses to therapy to include sub-clonal profiles
- Examining treatment strategies in high risk Multiple Myeloma patients to target depth of chromosomal abnormalities
- Reconsidering the impact of drug resistance in re-treatment decisions based on patient specific sub-clonal responses.
- Redefining Multiple Myeloma staging using clinical and molecular profiles.

Dr Fonseca discusses the role of genetic markers in determining prognosis and treatment of patients with Multiple Myeloma as well as the appropriate use of advanced biomarkers for monitoring patients with sub-clonal disease.

Download The Sub-clonal Nature of Multiple Myeloma: New revelations to Genetic Studies and Biomarker Research
– video and slides

State of the Art in Prognostication for patients with Multiple Myeloma

Saad Usmani, MD, FACP, University of Arkansas for Medical Sciences, Little Rock, Arkansas, USA

The aim of total therapy chemotherapy treatment is to wipe out clonal heterogeneity as soon as possible. However, the myeloma community is divided between those advocating disease cure versus disease control. This presentation looks at the impact of total therapy treatment on patient outcomes, including overall survival and progression-free survival, which support a disease cure approach.

Prospective, randomised trials comparing control and cure directed treatments are ongoing but there is an urgency to target high risk multiple myeloma patients based on a patient's level of 'genomic chaos'.

Dr Usmani highlights results demonstrating the effect of cytogenetics and gene expression profiling in Multiple Myeloma prognostication plus the need for imaging studies at diagnosis and relapse of disease. He also discusses the importance of future modeling technologies to include all suitable prognostic findings.

Download State of the Art in Prognostication for patients with Multiple Myeloma – video and slides

The Immunoglobulin Heavy/Light Chain assay – Diagnostic sensitivity, prognostic significance and role in monitoring therapy

Heinz Ludwig, MD, Medizinischen Abteilung für Onkologie und Hämatologie, Vienna, Austria

Hevylite assays measure both monoclonal immunoglobulin (mlg) levels as well as the isotype-matched and uninvolved, polyclonal immunoglobulin levels (uHLC).

Hevylite has two key advantages over current routine techniques:

- Allowing accurate quantification of mlg when electrophoresis techniques cannot provide results e.g. when the mlg co-migrates with other proteins or when the mlg is below 10g/L.
- Allowing investigation of mlg's that are negative by immunofixation. This is important at diagnosis and when monitoring disease for the determination of response and detection of relapse.

Prof. Ludwig discusses how **Hevylite** is important at both diagnosis and maximum (best) response in Multiple Myeloma.
At diagnosis, **Hevylite** is predictive of progression-free and overall survival. A more abnormal ratio indicates poorer prognosis. When used with Beta 2 Microglobulin, abnormal **Hevylite** ratios provide a prognostic model with better discrimination between at risk groups than the International Staging System (ISS model).
At maximum response, abnormal **Hevylite** ratios are indicative of decreased overall survival. This applies in immunofixation negative patients and can also indicate relapse before immunofixation becomes positive.

Also in this presentation uHLC pair suppression is highlighted as a novel indicator of MGUS progression.

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The Immunoglobulin Heavy/Light Chain assay – Diagnostic sensitivity, prognostic significance and role in monitoring therapy
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Disease Monitoring in Myeloma: The new and the old

Shaji Kumar, MD, Mayo Clinic, Rochester, Minnesota, USA

Why do we detect and monitor disease in myeloma?
How do we monitor tumour burden?
When and how often do we need to monitor?
What do we do with this information?
These are questions Dr Kumar aims to answer within this presentation.

After a short review of methods to detect monoclonal protein in monoclonal gammopathies, which also includes **Hevylite**®, Dr Kumar discusses the significance of:

- Bone marrow morphology, immunofluorescence microscopy and flow cytometry
- Immunoglobulin free light chain analysis
- Surface immunophenotypes and plasma cell phenotypes
- DNA content
- Proliferation by flow cytometry

He also reviews:

- Minimal residual disease (MRD) detection by flow cytometry and PCR
- The role of peripheral blood flow cytometry, cytogenetics and FISH in monoclonal disorders
- Results from imaging studies (CT/MRI/PET)

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Shaji Kumar, MD, Mayo Clinic, Rochester, Minnesota, USA

Following this, monoclonal disease evolution, response criteria, depth of response and MRD in relation to overall survival is presented. Criteria for relapse from complete response (CR) and progressive disease parameters are also defined.

Dr Kumar concludes that current markers allow monitoring of patients for development of disease, assessment of therapy effect and detection of relapse but finishes by mentioning which future, more sensitive, methods look the most promising.

Download Disease Monitoring in Myeloma: The new and the old – video and slides

Further Information, Request a DVD & Contacts

If you would like to request a DVD of the Symposium please complete the DVD request form

Visit our website for further information on the clinical use of **Freelite** and **Hevylite**.

If you have questions about running the serum free light chain or heavy/light chain test in your laboratory visit our **Freelite** or **Hevylite** web pages.

Or visit our online, free, educational resource with up to date information on **Freelite** and **Hevylite**:
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